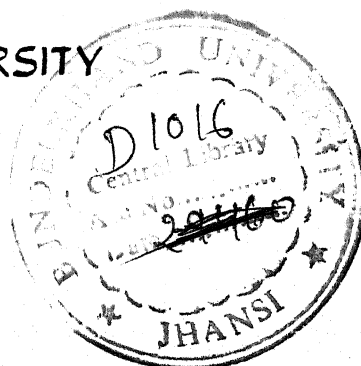


**EVALUATION OF BREAST DISEASES BY
FINE NEEDLE ASPIRATION CYTOLOGY
AND HISTOPATHOLOGY**

THESIS
FOR
DOCTOR OF MEDICINE
(PATHOLOGY)



BUNDELKHAND UNIVERSITY
JHANSI (U. P.)



C E R T I F I C A T E

This is to certify that the work entitled
"EVALUATION OF BREAST DISEASES BY FINE NEEDLE
ASPIRATION CYTOLOGY AND HISTOPATHOLOGY" being
submitted for M.D.(Pathology) has been carried out by
Dr. NARENDRA himself in this department.

He has put necessary stay in the department
as required by the regulation of Bundelkhand University,
Jhansi.



(R.K. GUPTA)

M.D., MNAMS,
Professor and Head
Department of Pathology,
M.L.B. Medical College,
Jhansi

Dated : 3.8.91

C E R T I F I C A T E

This is to certify that the work entitled "EVALUATION OF BREAST DISEASES BY FINE NEEDLE ASPIRATION CYTOLOGY AND HISTOPATHOLOGY" being submitted for M.D.(Pathology) has been carried out by Dr. NARENDRA under my guidance and supervision in the Department of Pathology. His observations and results have been checked and verified by me from time to time.

This work fulfils the basic ordinances governing the submission of thesis laid down by Bundelkhand University, Jhansi.


(RATNA)

M.D.,
Assistant Professor,
Department of Pathology,
M.L.B. Medical College,
Jhansi.

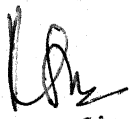
Dated : 3-8-91

(GUIDE)

C E R T I F I C A T E

This is to certify that the work entitled
"EVALUATION OF BREAST DISEASES BY FINE NEEDLE
ASPIRATION CYTOLOGY AND HISTOPATHOLOGY" being
submitted for M.D.(Pathology) has been carried out by
Dr. NARENDRA under our guidance and supervision in the
Department of Pathology. His observations and results
have been checked and verified by us from time to time.

This work fulfils the basic ordinances
governing the submission of thesis laid down by
Bundelkhand University, Jhansi.



(RAJEEV SINHA)
M.S.,
Assistant Professor,
Department of Surgery,
M.L.B. Medical College,
Jhansi

(CO-GUIDE)



(V.K. SHARMA)
M.D., DCP,
Assistant Professor,
Department of Pathology,
M.L.B. Medical College,
Jhansi

(CO-GUIDE)

Dated: 3.8.91

A C K N O W L E D G E M E N T

A C K N O W L E D G E M E N T

When I wish to express my heartfull thanks to those who helped me I have no words for it but only feelings. The upsurge of gratitute and love for their kind and loving co-operation in this project prostrates me before all of them.

The affectionate nature and heartening words of Prof. R.K.Gupta, M.D., MNAMS, Professor and Head, Department of Pathology, M.L.B. Medical College, Jhansi constantly provided me the confidence and enthusiasm, so essentially vital to such a project.

It was my proud privilage to have an opportunity to work under the supervision of Dr. (Mrs.) Ratna, M.D., Assistant Professor, Department of Pathology, M.L.B. Medical College, Jhansi. I am unable to express my feelings of gratitute for her constant help as she helped me at each and every stage of this project even at her personal inconveniences. Her interest and attention in this work were source of great inspiration to me.

I deeply express my heartfelt thanks to my co-guides Dr. V.K.Sharma, MD, DCP, Assistant Professor, Department of Pathology and Dr. Rajeev Sinha, M.S., Assistant Professor, Department of Surgery, M.L.B. Medical College, Jhansi.

They have been too kind to help me even at their personal inconvenience at every stage of this work.

I am very grateful to my parents, wife and brothers for their constant moral support.

I am thankful to Mr. Kanhaiya Lal for his neat type script of this project.

Dated : 3-8-91

Narendra
(NARENDRA)

C O N T E N T S

	<u>PAGE NO.</u>
INTRODUCTION -----	1 - 2
REVIEW OF LITERATURE -----	3 - 15
MATERIAL AND METHODS -----	16 - 23
OBSERVATION -----	24 - 33
DISCUSSION -----	34 - 41
CONCLUSION -----	42 - 44
BIBLIOGRAPHY -----	I - VI
SUMMARY -----	Attached separately

I N T R O D U C T I O N

For proper management of cases preoperative diagnosis of any tumour is essential. In fact most tumours can be diagnosed clinically with moderate degree of accuracy but the final diagnosis in every case is usually done by histopathology. However surgical incisional or excisional biopsy is essential for histopathological diagnosis. Surgical biopsy is an institutional, troublesome and time consuming procedure. So several methods of rapid diagnosis have been attempted to overcome this delay. For establishing a definite pathological diagnosis, the role of cytology is controversial. Fine needle aspiration cytology is one method among the present methods for cytological diagnosis.

Fine needle aspiration cytology is collection of cell sample from any palpable mass, superficial or deep in the body with help of fine needle and syringe by creating a vacuum. The aspirated cell sample is a suspension of various types of cells in minute amount of blood and tissue fluid.

Although the technique of the fine needle aspiration (FNA) to diagnose cancer was first used in the United State by Guthrie in 1921 but Martin and Ellis

(1930) are generally credited for introducing this technique. By 1934 they had performed over 1400 aspiration biopsies from various sites while including 280 breast cancers.

Fine needle aspiration cytology is a simple technique easy to perform without causing much discomfort to patient, safe, of low cost and excellent patient acceptance. It may be repeated from different sites of the representative areas. It is now widely accepted and successfully employed diagnostic procedure.

Carcinoma of breast is the 2nd most common neoplasm in the females in India and usually patient presented with a history of a palpable mass. So this mass is easily accessible for needle aspiration. Fine needle aspiration cytology provides a better diagnostic method to differentiate between benign or malignant breast lesion as well as form basis for early treatment.

R E V I E W O F L I T E R A T U R E

REVIEW OF LITERATURE

Aspiration biopsy cytology is the study of cells obtained by a fine needle under vacuum. The specimen consists of a minute quantity of tissue or fluid. The lesion may be palpable superficial or deep mass. Any area of body is a suitable target of aspiration biopsy.

Grieg & Gray (1904) were the first to employ aspiration procedure to obtain material from lymph nodes for studying the etiology of trypanosomiasis.

Guthrie (1921) reported the observations made on material collected by needle puncture and aspiration of lymph node in cases of Hodgkin's disease, acute and chronic myloid leukaemia and metastatic tumours as well as non neoplastic conditions like syphilis, tuberculosis and trypanosomiasis.

Martin and Ellis (1930) instituted a standard technique for needle aspiration in malignant tumours. They reported 65 cases of neoplastic diseases in which diagnosis had been made from aspirated material obtained by a 18 gauge needle and a syringe of 20 ml. The results had been checked and confirmed by histopathologic sections.

In 1933 Stewart, who had examined 500 aspirations, from breast and advocated its use for differentiation of various conditions like; fat necrosis, fibroadenoma, abscess and carcinoma.

By 1934, Martin and Ellis had performed over 1400 aspiration biopsies, including 280 breast cancers.

Needle aspiration was employed in breast lesion in 1959 by Gibson & Smith and smears were subjected to Haematoxylin and Eosin staining and on comparing with histological sections, they found 91.5% of accuracy in their study.

This needle aspiration technique although was safe and without any danger, but few had raised the possibility of implantation of cancer along the route of needle aspiration. But this doubt was removed and technique was found without any such ill effects by Franzen and Zajicek (1968), they had proved that there is essentially no danger of implantation of cancer with breast aspiration in their study of 3479 breast aspirates and no evidence of seedling along the needle tract was found.

According to Winship (1969) greater diagnostic accuracy can be obtained when the pathologist performs the procedure himself. During past 20 years 469 aspiration biopsies of breast cancer were performed with 92% accuracy in diagnosis in this study.

Zajdela et al (1975) performed aspiration cytology on 2772 breast masses, all of which subsequently had open biopsies of the 1745 histologically malignant tumours, 1539 (88%) had a concordant cytologic diagnosis, 54 (30%) were diagnosed as probably malignant, 63 (3.6%) were false negative and 80 (5.0%) had inadequate smears for diagnosis. Of the histologically benign lesions, 916 (89%) had a concordant cytology, only 3 (0.3%) were false positive. Cancer was suggested in 42 (4.0%) and smears were inadequate in 66 cases (6.4%). Very small or very large sized cancer and a high degree of differentiation were major causes of false negative aspirations.

Talukedar et al (1978) performed thin needle aspiration as compared to thick needle aspiration since the thick needle causes more trauma and resultant aspiration of blood may distort the results. He studied a series of 31 cases and diagnostic accuracy rate was more than 90%.

Kline et al (1979) published a review of 3545 cases of breast lump in which fine needle aspiration biopsy was done. They found abnormal cells in the aspirate from 90% of 368 malignancies. They further concluded that this method is rapid, accurate and essentially complication free and added that it could be used with the idea of complementing not competing with routine histological biopsies.

Kern (1979) performed fine needle aspiration on 93 breast carcinomas and concluded that a cytopathological diagnosis of carcinoma based on aspiration smears of the breast is highly accurate if strict criterians of malignancy are applied but normal smears from solid breast masses do not exclude malignancy.

In the another study, Kline (1981) published a review of 4241 aspirates from the breast in which fine needle aspiration biopsy was done. Of the 3809 benign lesions, 61 (1.6%) were interpreted as possibly malignant. In all excisional biopsy, not mastectomy, was recommended as the next procedure. More than 50% of these misdiagnosis were from aspirates of fibrocystic disease, 15% were from fibroadenomas and the reminder were from gynecomastia, solitary papillomas, periareolar hyperplasia, pregnancy hyperplasia and granulation tissue. Most errors were based on specimens that were insufficiently cellular or whose poorly preserved cells lacks the majority of the criteria of malignancy.

Abele et al (1983) have worked on fine needle aspiration of palpable breast masses. They used a three phase programme to acquire experience with fine needle aspiration while proceeding services for 205 patients

over 16 months period. They performed fine needle aspiration sequentially in vitro, in vivo and finally in vivo for clinical use.

In phase I, 63 breast masses were aspirated after surgical excision. All benign lesions were diagnosed by fine needle aspiration and confirmed by histopathology. No benign lesion were diagnosed by fine needle aspiration as malignant or suspicious. The single false negative diagnosis was for an acellular aspirate. Only 2 malignant cases were diagnosed as suspicious.

In phase II, 25 breast masses were aspirated in vivo on discrete lesions before biopsy and 25 additional unfixed surgical breast biopsy specimen submitted by other surgeons were aspirated. There was a single false negative diagnosis, which was apparently due to fine needle aspiration sampling error. Only one malignant case was diagnosed as suspicious.

In phase III, they used fine needle aspiration of breast masses as a clinical diagnostic tool. Initially, all malignant fine needle aspiration diagnosis were confirmed by surgical biopsy before definitive recommendation were made. All benign fine needle aspiration diagnosis were followed by clinical estimation with mamography as indicated. If a biopsy of a mass was performed by open methods, the mas^s

was included in benign group only after at least six months of the clinical follow up. In phase III, they performed 92 fine needle aspiration biopsies. The single false negative diagnosis was again for an acellular smear from a clinically suspicious lesion. Three malignant and two benign lesion were diagnosed as suspicious.

Wanebo et al (1984) have worked on fine needle aspiration cytology in lieu of open biopsy in management of primary breast cancer. They performed fine needle aspiration in 398 patients out of these 25% were positive for cancer while 8% were suspicious and 10% had unsatisfactory results. It was negative for cancer in 57% patients.

Frable (1984) have performed 853 aspiration biopsies of palpable breast masses by using 20 or 22 gauge needle and 20.0 ml syringe during the 9 years period. There were 269 diagnosis of breast cancer, 42 suspected cases of cancer and 496 aspirates reported as benign tumour, inflammation or another non neoplastic diagnosis. Twenty seven cases of carcinoma were not diagnosed from the aspiration biopsy sample. There was one false positive diagnosis of carcinoma in a patient whose tumour was a cystosarcoma phylloides, benign variant. Forty six aspirates were considered unsatisfactory, usually because of an insufficient

cellular sample. Sensitivity for the diagnosis of breast cancer was 89%, while specificity for the absence of breast cancer was 97%. Only 13 cases in the group reported as suspicious for carcinoma were proven not to be breast cancer after excisional biopsy and histologic study.

Wollenberg et al (1985) published a review of 321 cases with statistical evaluation in which fine needle aspiration cytology of breast was done. They found that their results for sensitivity, specificity, predictive value of a positive diagnosis and predictive value of a negative diagnosis were 65%, 100%, 100% and 89.6% respectively.

Smallwood et al (1985) has performed fine needle aspiration cytology in 480 breast lesions. With adequate smears aspiration cytology was 100% specific with no false positive diagnosis. Cytology was unsatisfactory in 36% of benign lesion owing to poor cellularity of the sample.

Eisenberg et al (1986) have performed aspiration biopsy of breast tumours before excisional biopsy or mastectomy. During a ten year period, 1942 aspiration biopsies of 1906 mammary tumours in 1874 patients were performed pre-operatively. Cytological findings were categorised as positive (1107 cases), suspicious (152 cases), atypical

(183 cases), benign (166 cases) and unsatisfactory (298 cases). All positive cases with follow up were confirmed histologically or by clinical examination. Ninety six per cent of the patients with suspicious, 86% with atypical, 51% with benign and 72% with unsatisfactory aspiration biopsies had malignant neoplasms on follow up. Aspiration smears obtained from ductal carcinoma showed marked pleomorphism and (69%) were cytologically positive. They had described that naked globoid nuclei in lymphocytic background permitted cytologic diagnosis of medullary carcinomas (84%). Papillary clustures in a mucinous background allowed cytologic diagnosis of colloid carcinomas (58%). Cytologic findings were positive in (32%) miscellaneous malignant mammary neoplasms. However, only (25%) lobular carcinomas were diagnosed on aspiration. Aspiration cytology diagnosed primary malignant mammary neoplasms (67%) and (68%) metastatic neoplasms of breast; if unsatisfactory cases are excluded these figures become (75%) and (76%) respectively. If those cases reported as suspicious are included with the positive cases and those reported as atypical are included with the negative cases, aspiration cytology would have a sensitivity of 84% for the presence of carcinoma, a specificity of 97% for the absence of carcinoma, a predictive value of 99% for a positive diagnosis and a predictive value of 56% for a negative diagnosis; the diagnostic efficiency would be 86%.

Silverman et al (1987) has performed 219 fine needle aspiration biopsies of the breast during the period of 1983 to 1985. The series consisted of 98.2% women and 1.8% men, with an age range of 14 to 90 years. The sensitivity of fine needle aspiration procedure was 82.2%, its specificity was 98.8% and over all efficiency of the test was 95.4%. The false negative rate was 4.4%, with no false positive diagnosis for the primary diagnosis of breast carcinoma.

Pandit et al (1988) has performed fine needle aspiration on 501 breast lumps. The cytological results were classified as inflammatory, granulomatous mastitis, fat necrosis, galactoceles, cyst, benign, suspicious and malignant. The subsequent histological examination was carried out in 264 cases. Both the results were correlated and it was found that fine needle aspiration cytology of breast was 94% accurate, 83% sensitive and 100% specific.

Langmuir et al (1989) has performed 280 fine needle aspirations on 257 palpable breast lesions in 200 patients. Fine needle aspiration cytology had a sensitivity of 96% and a specificity of 94% in these cases, there were no false positive diagnosis of cancer.

Douglas Jones et al (1989) has reported a case of breast carcinoma with tumour giant cells with fine needle aspiration cytology in a 31 years old woman presented with a cystic mass in the left breast. At fine needle aspiration the mass felt gritty and a firm mass remained after drainage of cyst. Cytologic examination of the aspirate showed mononucleated malignant cells and an array of bizarre malignant multinucleated giant cells. Subsequent histologic study of the lesion showed a central cystic cavity lined by bizarre tumour giant cells.

Srinivas et al (1989) has performed 222 fine needle aspirations on breast lesions. There were 205 satisfactory smears out of which 144 were benign lesions, 61 malignant lesions. Seventeen were unsatisfactory smears. Histopathology correlation was done in 126 benign lesions, 44 malignant lesions and 12 unsatisfactory smears. The cytological correlation for benign and malignant lesions was 91.09% and 91.6% respectively. There were false negatives which were due to extensive necrosis or due to scanty aspirate. There were no false positive in this study.

Wilkinson et al (1989) has done an analysis of 276 fine needle aspirates of the breast in 240 cases. Out of these cases, 108 underwent subsequent biopsy. Correlations between fine needle aspiration cytology and the surgical

pathological findings revealed that fine needle aspiration had a sensitivity of 79.4% specificity of 100% and a prediction value of positive diagnosis of 100%. The overall diagnostic accuracy was 92.4%.

Macansh et al (1990) has reported a case of granulation mastitis by fine needle aspiration cytology. A 24 year old pregnant woman presented with a six weeks history of a rapidly enlarging breast mass, considered clinically to be malignant. The fine needle aspiration smears contained numerous aggregates of epithelioid cells histiocytes, admixed with Langhan's and foreign body giant cells, lymphocytes, neutrophilic leucocytes and necrotic debris, leading to a diagnosis of granulomatous mastitis.

Gupta et al (1990) has reviewed 4739 needle aspirates of the breast, with an emphasis on the diagnosis of carcinoma in young women under the age of 30 years. Among benign diseases, fibroadenomas were most frequently seen in younger women (24.3% of 919 cases) while cysts were most frequently seen in women 30 years of age and older (20.0%). Fibrocystic conditions were identified in approximately 30% of women in each group. All younger women with suspicious diagnosis had fibrocystic disease at biopsy, in older women, 75% of the suspicious cases proved to be carcinomas while 25% proved to be fibrocystic diseases. Carcinomas were diagnosed cytologically in 1.3% of younger women and in 97% in older women.

Debnath (1990) has analysed 2936 breast aspirates followed by histopathological confirmation. He found 54.91% cases were malignant, 24.52% benign, 0.07% false positive, 0.24% false negative and 20.26% others.

Chen (1990) has reported a rare case of pure squamous cell carcinoma of the breast in which the diagnosis was initially suggested by fine needle aspiration cytology. Smears and cell blocks of the aspirate showed atypical keratinized cells admixed with inflammatory cells. The diagnosis was confirmed by open biopsy.

Roy et al (1990) had done fine needle aspiration cytology in 209 cases of breast lesions. The study revealed that fibrocystic disease of the breast out numbered (35%) all lesions, malignant lesions of breast and fibroadenoma (25.5% and 15% respectively) were next in order of frequency. Incidence of different types of lesions were almost equal in both breast having 40.7% and 41.2% incidence. Eighty seven of the total number of 209 cases were not confirmed by histopathological study. False observation was noted in 20 cases by subsequent histopathological examination. False positive was only 10% out of 20 and false negative were the bulk (90%).

Sidhu et al (1990) has reported follow up results of 132 out of a total of 200 aspirations performed on 182

breast lumps. The presence of adipose tissue in the smear has been interpreted. They found 31.28% aspirations as malignant, 8.33% suspicious, 49.24% benign and 10.60% scanty or acellular. Results were confirmed by histopathology. They found that in 11 suspicious aspirates 90.91% were malignant and 9.09% benign. No false negative result was obtained. Two false positive results obtained among 132 aspirations. Among scanty or acellular aspirates 14.29% were malignant and 85.71% were benign. Adipose tissue was present in all smears which were reported as malignant. There was an intimate mixing up of neoplastic and fat cells. Adipose cells were also seen in 20 benign smears but quantity was less and fat cells and epithelial cells were lying separately. Adipose tissue was not detected in aspirates of two cases of intraductal carcinoma which were cytologically reported as suspicious. Intimate mixing of neoplastic and fat cells represents infiltration of neoplastic cells into the surrounding fat. Because there is no such infiltration of fat by benign epithelial cells and fat does not form a part of benign tumour, fat is absent in the aspirate from such lesions. The presence of fat in small quantities in these cases could be due to the needle wandering away from the lump into the surrounding fat.

M A T E R I A L A N D M E T H O D S

MATERIAL AND METHODS

The present study was conducted in the Department of Pathology, Maharani Laxmi Bai Medical College & Hospital, Jhansi to evaluate the accuracy of fine needle aspiration cytology in the patients having palpable lumps in the breast. Patients attending surgical out patient department as well as admitted in surgical wards in one year period, were included in the study.

Patient's age, sex and clinical history was noted. Thorough general examination specially about anaemia, oedema and any clinical findings was done. Local examination of the breast was done about the size of the lump. Overlying skin of the lump along with nipple, areola was examined and any discharge was also noted. Lymphnode examination especially of axillary region was also done.

For rapid cytodiagnosis all patients, having breast lumps were subjected to fine needle aspiration. Most of the patients were also subjected to surgical incisional or excisional biopsy. Fine needle aspiration cytology results, were later compared with histopathological sections, stained with haematoxylin and eosin.

Fine needle aspiration cytodiagnosis was carried out as per following schedule.

Procedure :

The Fine Needle Aspiration was done by using 21 gauge disposable needle and 20 ml plastic disposable syringe. The syringe volume permits the establishment of adequate vacuum during aspiration. The skin overlying the lump was painted with 5% povidone iodine. The lump was held between the thumb and index finger of the left hand. The needle point was touched to the skin and its direction was determined before it was introduced into the mass in one swift motion. This minimizes discomfort to the patient. The use of anaesthesia was a matter of preference depending on patient's mental state, the depth of the lesion and whether repeated efforts must be required. Once the tumour was engaged (indicated by resistance to the needle) full vacuum was applied while the needle was moved back and forth in the mass with short strokes. The syringe was observed for appearance of any specimen. When this appeared (or after five or so strokes), the syringe piston trigger was slowly released and allowed to return to the neutral position. The needle was then withdrawn from the mass. The needle was temporarily removed from the apparatus, and

the syringe was filled with air by pulling back on the plunger. The needle re-attached. The specimen was expressed onto a glass slide and smeared with a second slide. It was then immersed in fixative i.e. in equal volumes of ether and absolute alcohol or in 95% methyl alcohol for 30 minutes. These slides were stained with haematoxylin and eosin and Papanicolaou's stain.

Staining of smears was done as below :-

PAPANICOLAOU'S STAINING METHOD

Fixed smears of fine needle aspiration were subjected to following procedure :-

- 95% ethyl alcohol - 1 minute to 24 hours
- Rinse in distilled water - 1 minute
(to ride slides of fixative)
- Harris's haematoxylin - 2 to 4 minute
- Rinse in distilled water - 2 minutes
- Acid alcohol (to differentiate) - 1 or 2 dips
- Rinse in distilled water - 5 to 10 minutes
- Wash in running tap water - 5 minutes
- 95% ethyl alcohol - 2 minutes
- O.G.- 6 - $1\frac{1}{2}$ to 2 minutes
- 95% ethyl alcohol - 4 dips (quick)
- 95% ethyl alcohol - 4 dips (quick)

- E.A. 65 - 2 to 3 minutes
- 95% ethyl alcohol - 4 dips (quick)
- 100% ethyl alcohol - 4 dips (quick)
- 100% ethyl alcohol - 4 dips (quick)
- Xylol - 1 minute
- Mounted in D.P.X.

2. HAEMATOXYLIN AND EOSIN METHOD :

Fixed smears of fine needle aspirate was subjected to the following procedure :-

- Absolute ethyl alcohol - 10 dips
- Absolute ethyl alcohol - 10 dips
- 95% ethyl alcohol - 10 dips
- 95% ethyl alcohol - 10 dips
- Tap water - 10 dips
- Harris haematoxylin - 3 to 7 minutes
- Tap water - 10 dips
- Acid alcohol - 4 to 5 dips
- Wash in running tap water - 10 to 15 minutes
- Eosin - 1 to 2 minutes
- Tap water - 1 to 2 minutes
- 95% ethyl alcohol - 10 dips
- 95% ethyl alcohol - 10 dips
- Absolute ethyl alcohol - 10 dips

- Absolute ethyl alcohol - 10 dips
- Xylol - 10 dips
- Xylol - 10 dips
- Mount in D.P.X.

CYTOLOGICAL EXAMINATION :

Then cytological smears were seen and interpretation was made on the following criteria (Hubert, 1978 and Kline, 1981):-

1. Inflammatory Lesions :

The gross aspirate is yellowish, semisolid material. The smear shows necrotic material along with neutrophils, foamy macrophages, lymphocytes, plasma cells and duct epithelial cells.

2. Granulomatous Mastitis :

The gross aspirate is whitish, semisolid material. Microscopically necrotic material, lymphocytes, histiocytes and many Langhan's and foreign body giant cells are found.

3. Fat Necrosis :

The smear shows eosinophilic amorphous material, adipose tissue cells of various sizes and neutrophils, lymphocytes, foamy macrophages.

4. Galactoceles :

The aspirate is thick milky white fluid. Microscopically cells are not evident.

5. Cyst :

The aspirate is abundant (5 ml or more), yellowish or greenish fluid. The smears are prepared from centrifuged deposit of the fluid and reveal foamy macrophages.

6. Benign :

The aspirate is scanty e.g. fibroadenoma, fibrocystic disease. The smear shows large branching, tight and flat clusters of uniform duct epithelial cells. Many bare spindle shaped nuclei (myoepithelial cells) are seen. In few cases connective tissue cells (fibrocytes), and large cells with abundant granular cytoplasm (apocrine cells) are present. The duct epithelial cells show uniform benign looking nuclei. The aspirate from the well differentiated cystosarcoma phyllodes is distinguished from the fibroadenoma only by clinical correlation.

7. Suspicious of Malignancy :

Microscopically the cellularity of smear is variable. The cells are not arranged in tight clusters, the nucleus is large and hyperchromatic. However, there is no unequivocal diagnosis of malignancy.

8. Malignant :

Typical carcinoma presents a gritty resistance to fine needle. The aspiration material is variable in amount. The cellularity in scirrhus carcinoma is poor, whereas smears are very cellular in other types of carcinoma. The back ground reveals eosinophilic granular material. Smear shows pleomorphic cells which are arranged in loose clusters and these clusters are composed of several super imposed layers of cells. Isolated cells shows high nucleocytoplasmic ratio, hyperchromatic nucleus with irregular nuclear membrane and dense chromatin clumps. Few to moderate number of lymphocytes surround the malignant cells in medullary carcinoma. The myoepithelial cells are absent.

HISTOLOGICAL EXAMINATION :

In those cases where tissue sections were studied after incisional or excisional biopsy, the following standard procedure was employed.

Tissues were fixed in 10% formal saline over night or more than over night depending upon size of tissue and they were subjected to process of dehydration, clearing and paraffin embedding so as to prepare paraffin blocks. These blocks were cut into thin sections ranging from 4 to 6 microns in thickness and stained with conventional haematoxylin and eosin method.

All the smears and sections prepared as above were examined under light microscope at different magnifications and diagnosis in each case was recorded (Symmers, 1978 and WHO, 1981).

All the cytological results were correlated with histological results. With the help of cytohistological correlation, sensitivity, specificity and predictive value of a positive aspiration for breast cancer were calculated as following (Frable, 1984) :

$$\text{Sensitivity (\%)} = \text{Positive in disease; } \frac{TP}{TP + FN} \times 100$$

$$\text{Specificity (\%)} = \text{Negative in disease; } \frac{TN}{TN + FP} \times 100$$

$$\text{Predictive value of a positive result (\%)} = \frac{TP}{TP + FP} \times 100$$

Where, TP = True positive,
 TN = True negative,
 FP = False positive,
 FN = False negative

O B S E R V A T I O N S

O B S E R V A T I O N

The present study was conducted in the Department of Pathology, M.L.B. Medical College & Hospital, Jhansi in the patients having palpable lumps in the breast. Patients attending surgical out patient department as well as admitted in surgical wards in one year period, were included in the study. It comprises of analysis of forty patients of palpable lumps in the breast.

Fine needle aspiration cytology was performed in all the cases and cytological evaluation was done, which was correlated with histopathology in maximum cases. Following observations were made :-

TABLE NO. I

Showing distribution of cases according to age.

S.No.	Sex	No. of cases	percentage
1-	Male	2	5.0
2-	Female	38	95.0
Total		40	100.0

This table showed that incidence of breast lesions was maximum (95%) in females and minimum in males (5%).

TABLE NO. II

Showing distribution of cases according to age.

S.No.	Age (In years)	No.of cases	Percentage
1-	11 - 20	9	22.5
2-	21 - 30	12	30.0
3-	31 - 40	8	20.0
4-	41 - 50	8	20.0
5-	51 - 60	3	7.5
TOTAL		40	100.0

This table showed that incidence of breast lesions was maximum in third decade and then there was a gradual decline.

TABLE NO. III

Showing involvement of right or left breast.

S.No.	Breast involved	No.of cases	Percentage
1-	Right	17	42.5
2-	Left	19	47.5
3-	Both	4	10.0
Total		40	100.0

This table showed that incidence of breast lesions was nearly same in left breast as in right breast. Both breast were involved in 4 cases.

TABLE NO. IV

Showing distribution of cases according to quadrant of breast

S.No.	Quadrant of breast involved	No. of cases
1.	Upper lateral quadrant	32
2.	Lower lateral quadrant	10
3.	Upper medial quadrant	9
4.	Lower medial quadrant	8
5.	Nipple and areolar region	8

This table showed that involvement of upper lateral quadrant was maximum i.e. in 32 cases, involvement of lower lateral quadrants in 10 cases, upper medial quadrant was in 9 cases, lower medial quadrant was in 8 cases, nipple and areolar region was in 8 cases.

Note :- In 5 cases all quadrants, in 3 cases both upper and lower lateral quadrants, in 2 cases, both upper lateral and upper medial quadrants, and in 2 cases both lower medial and upper medial quadrants were involved.

TABLE NO. V

Showing the clinical findings of cases studied
(Total number of cases are forty)

Clinical diagnosis	No.of cases	Clinical appearance		Consistency			Dis-charge	Ulceration	Con-dition of nipple and areola	Axillary node
		Mobile	Fixed	Soft	Firm	Hard				
<u>Non-neoplastic</u>										
(a) Inflammatory	4	4	Nil	4	Nil	Nil	Nil	Nil	Normal	Nil
(b) Non-inflammatory	3	3	Nil	3	Nil	Nil	Nil	Nil	Normal	Nil

<u>Neoplastic</u>										
a) Benign	14	14	Nil	13	01	Nil	01	Nil	Normal	Nil
b) Malignant	12	10	02	01	10	01	01	01	Ulcerated (1)	10

Lump	07	07	Nil	05	02	Nil	01	Nil	Normal	01

From the above table, we can obtain results about clinical presentation.

All the non-neoplastic lumps were mobile and soft in consistency and no other abnormalities like discharge, ulceration were found. Nipple and areola were normal in all cases. Axillary lymphnodes were not involved in any case.

Out of 14 benign lumps, all lumps were mobile and soft except one which was firm. Yellowish discharge from nipple was present in one case. Axillary lymph node was not enlarged in any case.

All malignant lumps were mobile except two lumps which were fixed. They all were firm except one soft and one hard lump. Watery discharge and ulceration was present in one case with ulcerated nipple and areola. Axillary lymph nodes were enlarged in all cases except two cases.

Seven swellings were diagnosed clinically as breast lumps. They were all mobile and soft except two which were firm. Serous discharge from nipple was present in one case while axillary lymph nodes involvement was also present in one case.

TABLE NO. VI

Showing different types of lesions diagnosed by fine needle aspiration cytology.

S.No.	Pathological condition	No.of cases	Percentage
1.	Non-neoplastic :		
	Inflammatory	05	12.5
	Non-inflammatory	04	10.0
2.	Neoplastic :		
	Benign	15	37.5
	Malignant	15	37.5
3.	Inadequate aspirate	01	2.5
Total		40	100.0

Table VI shows equal incidence of benign and malignant cases. 22.5% cases were of non-neoplastic in nature including inflammatory and non-inflammatory cases. In one case aspirate was inadequate.

TABLE NO. VII

Showing lesions diagnosed by histology.

S.No.	Pathological condition	No.of cases	Percentage
1.	<u>Non-neoplastic :</u>		
	(a) Inflammatory		
	-Chronic mastitis (Non specific)	01	2.9
	- Chronic granulomatous mastitis (Non tubercular)	01	2.9
	(b) <u>Non-inflammatory :</u>		
	- Galactoceles	01	2.9
	- Gynaecomastia	02	5.9

(2)	<u>Neoplastic :</u>		
	(a) <u>Benign</u>		
	- Fibroadenoma	11	32.4
	- Chronic cystic mastitis	03	8.8
	- Cystosarcoma phyllodes	01	2.9
	- Fibrocystic disease	01	2.9
	(b) <u>Malignant</u>		
	- Infiltrating duct adenocarcinoma	08	23.5
	- Medullary carcinoma	02	5.9
	- Intraductal carcinoma (Scirrhus)	01	2.9
	- Squamous cell carcinoma	02	5.9

	Total	34	100.0

NOTE : Tissues were available only in 34 cases.

Table VII showed distribution of various cases according to pathological diagnosis done by histopathology in 34 cases.

Non-neoplastic inflammatory conditions were found in 2 cases, one was chronic mastitis (non-specific) and other was chronic granulomatous mastitis (non-tubercular). Three cases were of non-neoplastic non inflammatory conditions, in which one was galactoceles and other two were gynaecomastia.

Twenty nine cases were neoplastic including both benign and malignant cases. Out of 29 cases, 16 were benign and 13 were malignant.

In 16 benign cases, 11 were fibroadenoma, 3 chronic cystic mastitis, one case of cystosarcoma phyllodes and one case of fibrocystic disease.

In 13 malignant cases, 8 were infiltrating duct adenocarcinoma, 2 medullary carcinoma, 2 squamous cell carcinoma and one was intraductal carcinoma (Scirrhus).

TABLE NO. VIII

Showing cytohistological correlation

S.No.	Pathological condition	No. of cases		Percentage of accuracy
		Aspira- tion	Histopa- thology	
1.	<u>Non-neoplastic :</u>			
	Inflammatory	02	02	100.0
	Non inflammatory	03	03	100.0
2.	<u>Neoplastic :</u>			
	Benign	15	16	93.8
	Malignant	13	12	92.3

NOTE :- Tissues were available only in 34 cases for histopathology.

Fine needle aspiration cytology provided diagnostic accuracy in establishing the correct diagnosis of non neoplastic inflammatory, non-neoplastic non inflammatory, benign and malignant lesions were 100%, 100%, 93.8% and 92.3% respectively. In one malignant case aspiration was inadequate. Overall diagnostic accuracy was 96.97%.

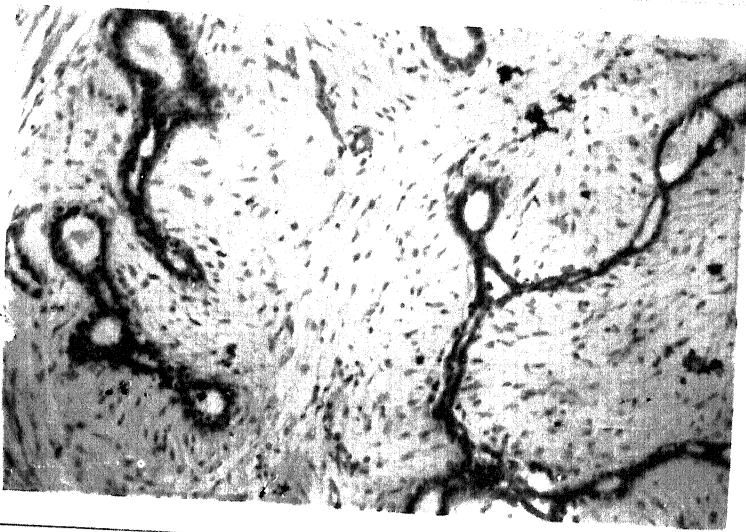
TABLE NO. IX

Showing specificity and sensitivity of breast fine needle aspiration cytology.

Fine needle aspiration (FNA) diagnosis	Histopathological diagnosis		
	Carcinoma present	Carcinoma absent	Total No. of cases
Malignant	12	01	13
Benign	0	15	15
Total	12	16	28

Sensitivity	:	100%
Specificity	:	93.8%
Predictive value of a positive diagnosis	:	92.3%

According to above table true positive, true negative, false positive and false negative cases were 12, 15, 01 and zero respectively. So sensitivity, specificity and predictive value of a positive diagnosis were 100%, 93.8% and 92.3% respectively.



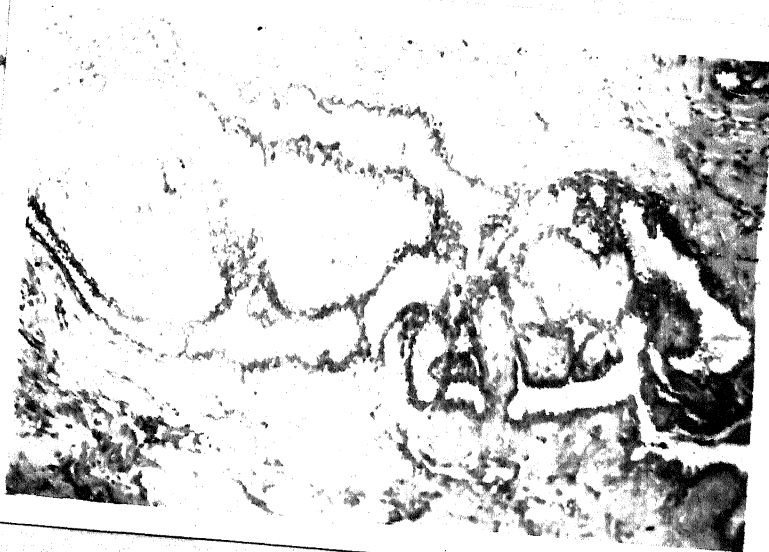
Microphotograph showing histopathology
of fibroadenoma breast (H & E x 70)



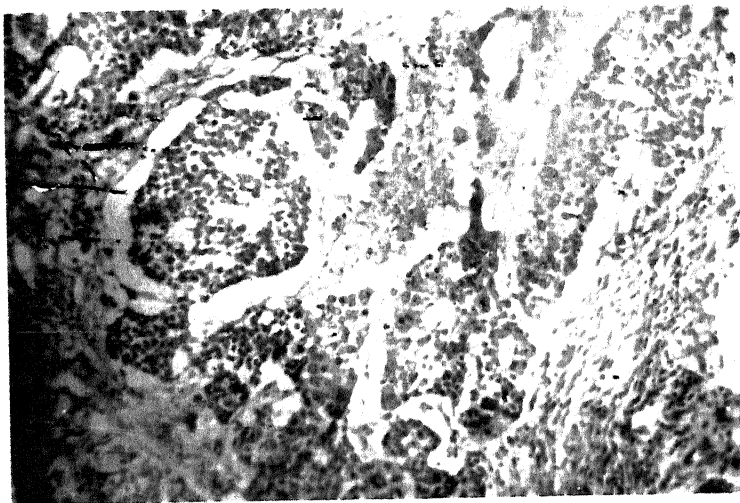
Microphotograph showing histopathology
of gynaeconastia breast (H & E x 70)



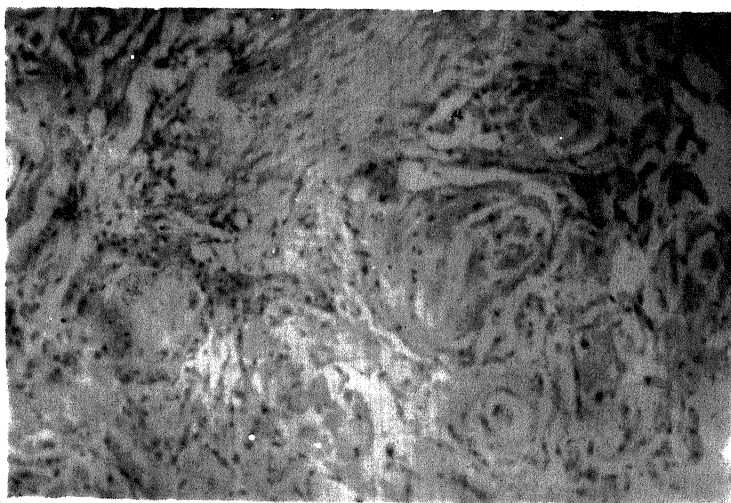
Microphotograph showing histopathology
of chronic cystic mastitis breast
(H & E x 70).



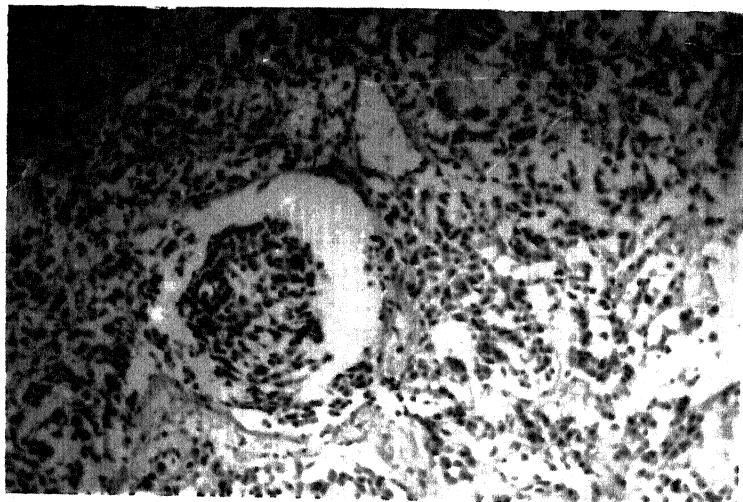
Microphotograph showing histopathology
of cystosarcoma phyllodes breast
(H & E x 70).



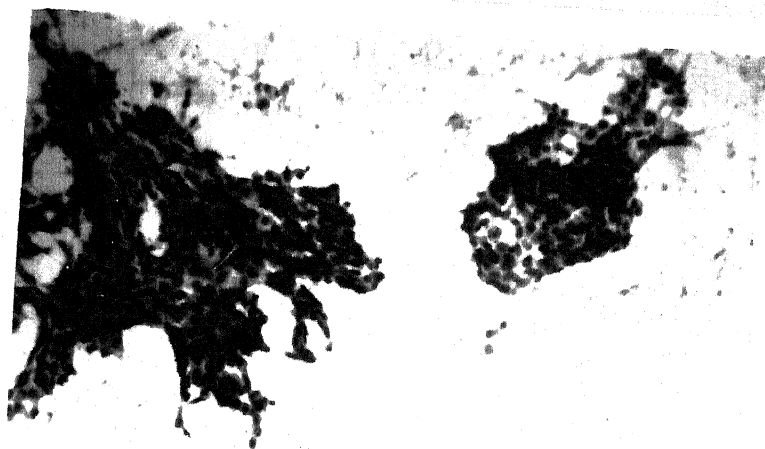
Microphotograph showing histopathology
of infiltrating duct adenocarcinoma
breast (H & E x 70).



Microphotograph showing histopathology
of squamous cell carcinoma breast
(H & E x 70).



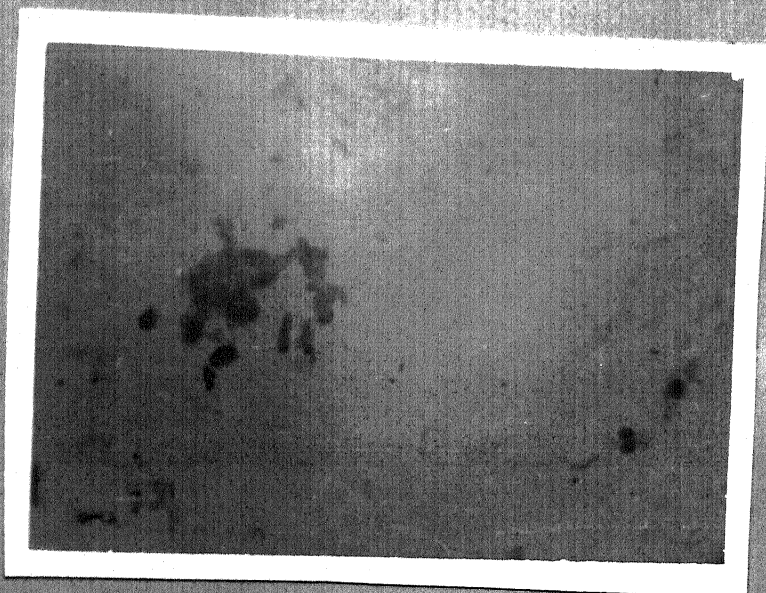
Microphotograph showing histopathology of medullary carcinoma breast (H & E x 70).



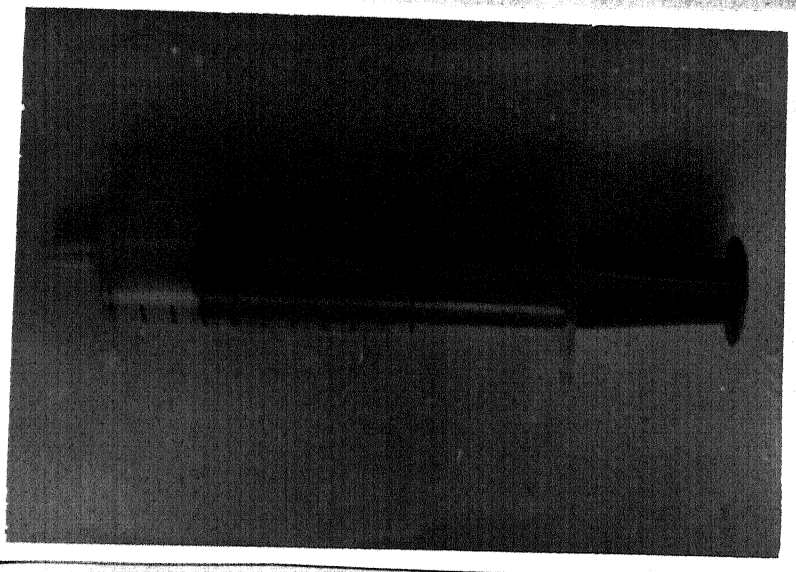
Microphotograph of fine needle aspiration cytology of breast showing big rounded cells having large nuclei with marked pleomorphism. Cells arranged in clumps suggesting an acinar pattern as seen in adenocarcinoma. (Papanicolaou's stain x 70).



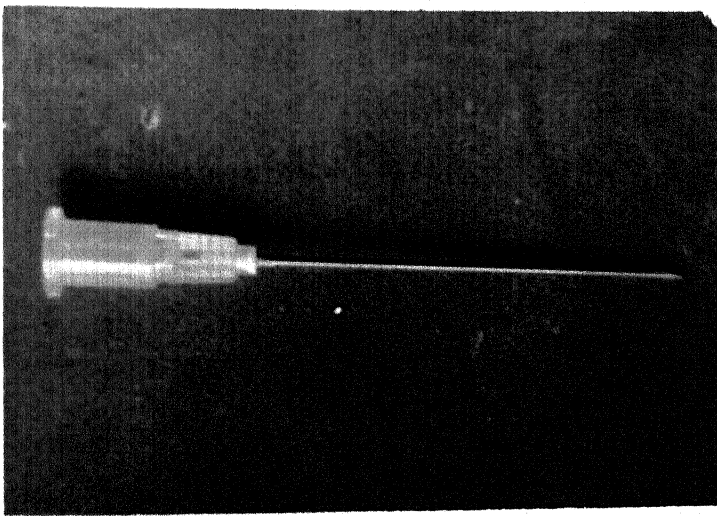
Microphotograph of fine needle aspiration cytology of breast showing big rounded cells having large nuclei with marked pleomorphism. Cells arranged in clumps suggesting an acinar pattern as seen in adenocarcinoma. (Papanicolaou's stain x 280).



Microphotograph showing fine needle aspiration cytology of fibroadenoma breast consisting of clumps of rounded cells of uniform size having benign looking nucleus (Papanicolaou's stain x280)



Photograph showing syringe of 20 ml
used for fine needle aspiration.



Photograph of hypodermic needle gauge 21
used for fine needle aspiration.

D I S C U S S I O N

DISCUSSION

A lump in the breast may be non-neoplastic or neoplastic. Non-neoplastic conditions may be either inflammatory or non-inflammatory. Neoplastic conditions may be either benign or malignant. As mentioned earlier the main role of fine needle aspiration cytology is to have a ready made, quick and accurate differentiation between benign and malignant lesions, so that further operative and palliative treatment may be chalked out.

Breast is one of the important site of malignancy in women. It is being observed now a days that incidence of breast carcinoma is increasing in India also, not only in nullipara and unipara but their frequency is stepping up on in cases of nullipara. Probably because of the fact that in the present environment majority of women refuse to give the advantage of breast finding to their sublings. The religious as well as scientific rules agree that breast feeding minimises the chances of cancerous development in the breast. On the other hand many times breast cancers are occult so much so that attention is drawn to the secondary, not to the primary, particularly when the lady is having

a small suckling child who can inflict trauma to the breast. In such circumstances even if lump is detected in the breast, it is ignored for a long time and designated as inflammatory swelling.

Under the above circumstances the importance and priority of fine needle aspiration cytology can easily be imagined. Rather in all cases with the recognition of lump whether suspected inflammatory or otherwise, if subjected to any surgical maneuver should be given a chance for fine needle aspiration cytology diagnosis before taking extensive exploratory surgical measures.

The present study is based on 40 cases of breast lumps. These patients were selected from the out patient department and in patient department of Surgery of M.L.B. Medical College & Hospital, Jhansi.

It is evident from Table No. I of the observations that incidence of breast lesions were predominantly confined to females (95%) than males (5%). Higher incidence of breast lesions in females were found because male breast is a rudimentary structure relatively insensitive to endocrine influences and apparently resistant to neoplastic growth while in females breast structure is more complex, greater breast volume and the extreme sensitivity to endocrine influences, all predispose this organ to a number of

pathological conditions (Robbins, 1989). Silverman et al (1987) have been reported that incidence of breast lump was 98.2% in women while 1.8% in men.

Table No. II showed that breast lesions were mostly found in 2nd decade to 5th decade. Pandit et al (1988) have been reported that majority of patients in their study were middle aged except four adolescent girls.

According to Table No. III incidence of breast lesions was nearly same in left breast and right breast. Roy et al (1990) have been also reported that incidence of different types of lesion were almost equal in both breast.

Table No. IV showed maximum incidence of breast lesions were seen in upper outer quadrant. The incidence of breast lesions were seen near about same in rest quadrants of breast. Eisenberg et al (1986) reported that the highest incidence of mammoary carcinoma was seen in the left breast and its upper outer quadrant. The next most frequently involved quadrant right or left breast, was the upper inner quadrant, followed by the lower outer quadrant and subereolar areas. The lower inner quadrant was least involved.

According to Table No. V most of the lesions clinically diagnosed as non neoplastic and neoplastic benign were mobile and soft while those diagnosed clinically as malignant were mobile and firm. Only two clinically malignant cases were fixed to chest wall. Ulceration was present in only one malignant case.

Table No. VI, VII and VIII indicate about fine needle aspiration diagnosis, histopathological diagnosis (of 34 cases in which tissues were available for histology) and cytohistopathological correlation.

With the help of fine needle aspiration, inflammatory non-neoplastic and non-inflammatory non neoplastic conditions of breast were diagnosed with 100% accuracy when compared with paraffin sections histopathology. Inflammatory non-neoplastic condition were of chronic mastitis (non-specific), chronic granulomatous mastitis (non-tubercular) were 2.9% each. Fine needle aspiration was also done in two cases of breast abscess in which only pus was present in the aspirates and no tissue was available for histopathology. Non-inflammatory non-neoplastic conditions were of galactoceles and gynaecomastia were 2.9% and 5.9% respectively. Differentiation between inflammatory non-neoplastic and non-inflammatory non-neoplastic conditions was also possible by examining the presence of polymorphs, lymphocytes and

other mononuclear cells. In the aspirates of galactoceles only milk was present. Aspirates of gynaecomastia were scanty, consist of mainly normal looking ductular epithelium in clusters.

The differentiation of neoplastic conditions into benign and malignant by aspiration cytology was also possible. Ninety three point eight percent (93.8%) accuracy was observed in diagnosing benign lesions when compared with paraffin section histopathology. The benign conditions were of fibroadenoma, chronic cystic mastitis, cystosarcoma phyllodes and fibrocystic disease were 32.4%, 8.8%, 2.9% and 2.9% respectively. The aspirates of benign lesions were scanty and showed tight clusters of uniform duct epithelial cells. Many bare spindle shaped nuclei (myoepithelial cells) were also seen. The duct epithelial cells showed uniform benign looking nuclei. One case of benign cystosarcoma phyllodes came with massive enlargement of left breast. The percentage of accuracy in benign lesions reported by Zajicek et al (1970), Stavic et al (1973), Gupta et al (1979), Bansal et al (1985) and Shreenivas et al (1989) were 97.1%, 93.66%, 96.29%, 97.87% and 91.09% respectively.

Ninety two point three percent (92.3%) accuracy was observed in diagnosing malignant lesions when compared with paraffin section histopathology. The malignant conditions were of infiltrating duct adenocarcinoma, medullary carcinoma, intraductal carcinoma (Scirrhou) and squamous cell carcinoma were 23.5%, 5.9%, 2.9% and 5.9% respectively. Lump of scirrhou carcinoma was hard in consistency. The aspirated material was variable in amount. The cellularity in scirrhou carcinoma was poor, whereas the smears were very cellular in other types of carcinoma. These cells were pleomorphic in size and shape. The cell clusters were loosely arranged and were composed of several superimposed layers of cells. Isolated cells showed high nucleocytoplasmic ratio, hyperchromatic nucleus with irregular nuclear membrane. The percentage of accuracy reported in malignant lesions by Furnival et al (1975), Vilaplanna et al (1975), Kline and Neal (1976), Gupta et al (1979), Bansal et al (1985) and Shreenivas et al (1989) were 96.1%, 94.3%, 89.8%, 97.8%, 94.34% and 91.6% respectively.

In one case, which on histopathological examination was labelled as fibrocystic disease of breast was wrongly diagnosed as malignant on aspiration cytology. Marked cellularity, moderate degree of variation in size and shape of cells and hyperchromatic nuclei were accounted for this error.

Fine needle aspirate was inadequate in one case (2.5%) which was diagnosed as malignant by histopathological examination. In this aspirate no cell was present except red blood cells. The percentage of inadequate aspirate reported by Pandit et al (1988) was 2.59%. In this case, aspirate was inadequate because lump was very large. According to Zajadela et al (1975) false negative and inadequate smears were more common in small and very large tumours.

Percentage of non-neoplastic, benign, malignant and inadequate aspirate were 22.5%, 37.5%, 37.5% and 2.5% respectively. Debnath (1990) have been reported 54.9% cases were malignant, 24.54% benign, 0.07% false positive, 0.24% false negative and 20.26% others.

There was no statistical difference on Papanicolaou's and Haematoxylin and Eosin staining, employed in present study but even the nuclear details were more prominent in Papanicolaou's staining as compared to Haematoxylin & Eosin. Overall diagnostic accuracy with these stains was 96.97%. Gibson & Smith (1959) presented with 91.5% diagnostic accuracy with Haematoxylin & Eosin by aspiration. Krauzer (1976) and Kline (1979) were reported 97.9% and 95.6% diagnostic accuracy respectively by Papanicolaou's staining. Pandit et al (1988) and Wilkinson et al (1989) have reported 94% and 92.4% diagnostic accuracy.

According to Table No. IX, sensitivity, specificity and predictive value of a positive diagnosis of fine needle aspiration cytology were 100%, 93.8% and 92.3% respectively. Sensitivity reported by Frable (1984), Wollenberg et al (1985), Pandit et al (1988) and Wilkinson et al (1989) were 89%, 65%, 83% and 79.4% respectively. Specificity reported by Frable (1984) was 97% and by Wollenberg et al (1985), Pandit et al (1988) and Wilkinson et al (1989) was 100%. Predictive value of a positive diagnosis reported by Frable (1984) was 95% and by Wollenberg et al (1985), Pandit et al (1988) and Wilkinson et al (1989) was 100%.

The aspiration technique in the present study has been found to be a significant method of rapid cyto-diagnosis of lesions of breast. It has also proved to be a safe, simple and feasible procedure and could be done single handed with a single set of instruments. It neither required hospitalization nor causes any complication. This simple technique can safely be repeated several times in the same patient. It appears to be a quicker and accurate method of diagnosis in experienced hands. Kline (1979) was of the opinion that this method is complementing and not competing with routine histopathological biopsies.

C O N C L U S I O N S

From the present study of Fine Needle Aspiration Cytology the following conclusions have been drawn :-

- 1- Aspiration cytology is simple and safe procedure for rapid cytodiagnosis. It is easily accepted by the patient. No surgical skill like incisional or excisional biopsy is required and there is no major complication in any case and also there is no need of any premedication for needle aspiration cytology.
- 2- There is no need of general anaesthesia for fine needle aspiration.
- 3- It can be repeated from different sites of the same patient without causing any appreciable discomfort. The technique can be adopted as an out door procedure and thus the problem of hospitalization can be overcome by fine needle aspiration cytology.
- 4- The smears can be made easily and if needed repeated samples for the subsequent follow up examination can be obtained.
- 5- This method is inexpensive and required simple laboratory procedure and at the same time comparing well with the more tedious and expensive histopathological examination.

- 6- Because of rapidity of technique in obtaining the results, treatment can be planned out at an early stage. The morbidity and mortality can thus be reduced appreciably especially in malignant tumours.
- 7- In the present series results of aspiration cytology were found to be encouraging in non-neoplastic and neoplastic lesions. The accuracy being 100% for non neoplastic, 93.8% for benign and 92.3% for malignant lesions. Thus the success rate of aspiration cytology in non neoplastic lesions was higher than neoplastic lesions.
- 8- Fine needle aspiration is valuable in differentiating benign from malignant lesions but is less valuable for typing of the tumour which however can be obtained from histopathological sections.
- 9- It was also observed in the present study that Papanicolaou's technique of staining is superior to Haematoxylin and Eosin staining method for staining needle aspirate in defining the cytological nuclear details for accurate diagnosis. No statistical significant differences between Papanicolaou's staining and Haematoxylin and Eosin staining method was observed in the present study.

- 10- In this study sensitivity, specificity and predictive value of a positive diagnosis were 100%, 93.8% and 92.3%.

From the all above conclusive points, procedure can be introduced for routine investigation in out patient and admitted cases, for quick and reliable diagnosis.

B I B L I O G R A P H Y

B I B L I O G R A P H Y

1. Abele, J.S., Miller, T.R., Goodson III, W.H., Hunt, T.K., Hohn, D.C. : Fine needle aspiration of palpable breast masses. A program for staged implementation. Arch. Surg. 118 : 859-863, 1983.
2. Bansal, R.L., Sankaran, V. and V^aliath, A.J. : Role of fine needle aspiration cytology in the diagnosis of breast lumps and its histopathological correlation. J. Cytol. 2 : 62-66, 1985.
3. Chen, K.T.K. : Fine needle aspiration cytology of squamous cell carcinoma of the breast. Acta Cytologica, 34 (5) : 664- 668, 1990.
4. Debnath, S.K. : Breast lump - experience of aspiration cytological diagnosis with 2936 cases. Indian Medical Gazette : 284-285, Sept, 1990.
5. Douglas - Jones, A.G., Barr, W.T. : Breast carcinoma with tumour giant cells. Report of a case with fine needle aspiration cytology. Acta Cytologica, 33 (1) : 109 - 114, 1989.
6. Eisenberg, A.J., Hajdu, S.I., Wilhelmus, J., Melamed, M.R., Kinne, D. : Preoperative aspiration cytology of breast tumours. Acta Cytologica, 30 (2) : 135-146, 1986.
7. Frable, W.J. : Needle aspiration of breast. Cancer 53 : 671 - 676, 1984.

8. Franzen, S. and Zajicek, J. : Aspiration biopsy in diagnosis of palpable lesions of the breast. *Acta. Radiol.* 7 : 241 - 262, 1968.
9. Furnival, C.M., Hughes, H.E., Hocking, M.A., Reid, M.M.W. and Bluggart, L.H. : Aspiration cytology in breast cancer, its relevance to diagnosis. *Lancet*, 2 : 446- 448, 1975.
10. Gibson, A. and Smith, G. : Aspiration biopsy of breast tumours. *Brit. J. Surgery*, 45 : 236-239, 1959.
11. Grieg, E.D.W. and Gray, A.C.H. : Note on lymphatic glands in sleeping sickness. *Lancet*, 1 : 1570, 1904.
12. Gupta, R.K., Dowle, C.S., Simpson, J.S. : The value of aspiration cytology of the breast, with an emphasis on the diagnosis of breast disease in young women below the age of 30. *Acta Cytologica*, 34 (2) : 165 - 168, 1990.
13. Gupta, S.K., Gosh, A.K., Choudhary, T., Dutta, T.K., Talwar, B.L. and Dutts, B.N. : Aspiration cytology in diagnosis of breast cancer. *Ind. J. Cancer*, 16 : 1-8, 1979.
14. Guthrie, C.G. : Gland puncture as a diagnostic measure. *Bull Johns Hopkins Hosp.*, 32 : 264-269, 1921. Quoted by Wanebo, H.J., Feldman, P.S., Wilhem, M.C., Covell, J.L., Binns, R.L. : *Ann. Surg.*, 199 : 569 - 579, 1984.
5. Hubert Schondrof (Translated by Volker Schneider); *Aspiration cytology of the breast*, 1st edition, page 67-91, London, W.B. Saunders Company, 1978.

16. Kern, W.H. : The diagnosis of breast cancer by fine needle aspiration smears. JAMA 241 : 1125-1127, 1979.
17. Kline, T.S. and Neal, H.S. : Needle aspiration of the breast - Why bother ? Acta Cytol. 20 : 324-327, 1976.
18. Kline, T.S., Joshi, L.P. and Neal, H.S. : Fine needle aspiration of the breast, diagnosis and pit falls : a review of 3545 cases. Cancer, 44 : 1458-1464, 1979.
19. Kline, T.S. : Masquerades of malignancy, a review of 4241 aspirates from the breast. Acta Cytologica 25 (3): 263-266, 1981.
20. Kline, T.S. : Handbook of Fine Needle Aspiration Biopsy Cytology, pages 114-175, St. Louis, Toronto, London, 1981.
21. Krauzer, G. and Boquoi, R. : Aspiration biopsy cytology, mamography and clinical exploration : A modern set up in diagnosis of tumours of breast. Acta Cytologica, 20: 319, 1976.
22. Langmuir, V.K., Cramer, S.F., Hood, M.E. : Fine needle aspiration cytology in the management of palpable benign and malignant breast disease. Correlation with clinical and mammographic findings, Acta Cytologica, 33 (1) : 93-98, 1989.
23. Macansh, S., Greenburg, M., Barraclough, B., Pacey, F. : Fine needle aspiration cytology of granulomatous mastitis. Report of a case and review of the literature. Acta Cytologica, 34 (1): 38 - 42, 1990.

24. Martin, H., Ellis, E. : Biopsy by needle puncture and aspiration. *Ann. Surg.*, 92 : 169 - 181, 1930.
25. Martin, H., Ellis, E. : Aspiration biopsy. *Surg. Gynaecol. Obst.*, 59 : 578 - 589, 1934.
26. Pandit, A.A., Maykar, R.S., Candes, F.P. : Fine needle aspiration cytology of the breast tumour. *Indian Journal of Cancer*, 25 : 136 - 143, 1988.
27. Robbins, S.L., Cotran, R.S., and Kumar, V. : Robbins pathologic basis of diseases, 4th edition, pages 1181-1204, W.B. Saunders Company. Philadelphia, London, Toronto, Montreal, Sydney, Tokyo, 1989.
28. Roy, M., Sanyal, M.K., Dasgupta, S., Sanyal, S., Bhattacharjee, A. : Fine needle aspiration cytology of breast lesions : An assessment, *Journal of Obstetrics and Gynaecology of India*, 40 (5) : 702 - 705, 1990.
29. Shreenivas, M., Kumar, G.H., Reddy, S.J.B., Bhaskaran, C.S. : Role of fine needle aspiration cytology in the diagnosis of breast lumps and its histopathological correlation. *Indian J. Pathol. Microbiol.* 32 : 133-137, 1989.
30. Sidhu, B.S., Kahlon, S.K., Kahlon, S.S. : Aspiration cytology in the diagnosis of breast lumps, *Indian Journal of Surgery*, 52 (10-11) : 503-507, 1990.
31. Silverman, J.F., Lannin, D.R., O'Brien, K., Norris, H.T. : The triage role of fine needle aspiration biopsy of palpable breast masses. Diagnostic accuracy & casr effectiveness. *Acta Cytologica*, 31 (6) : 731 - 736, 1987.

32. Smallwood, J., Herbert, A., Guyer, P., Taylor, I. : Accuracy of aspiration cytology in the diagnosis of breast disease. Br. J. Surg., 72 : 841 - 843, 1985.
33. Staviz, G.D., Tevur, D.T., Kajtandijive, D.R., Navak, J.J. : Aspiration biopsy cytologic method in diagnosis of breast lesions. Acta Cytologica, 17 : 188 - 190, 1973.
34. Stewart, F.W. : The diagnosis of tumours by aspiration. Am. J. Pathol. 9 : 801 - 812, 1933.
35. Symmers, W. St. C. : Systemic pathology, Second edition. Edited by W. St. C. Symmers, Volume 4, pages 1759-1861, Churchill Livingstone Edinburgh, London and New York, 1978.
36. ^uTalkedar, B.C., Roy, J.C. and Talukedar, G. : Thin needle aspiration biopsy as a diagnostic aid for breast tumours. Ind. J. Cancer, 15 : 1, 1978.
37. Villaplanna, E.V. and Jimenez - Ayalam : The cytologic diagnosis of breast lesions. Acta Cytologica 19 : 519-526, 1975.
38. Wanebo, H.J., Feldman, P.S., Wilhelm, M.C., Covell, J.L., Binns, R.L. : Fine needle aspiration cytology in lieu of open biopsy in management of primary breast cancer. Ann. Surg., 199 : 569 - 579, 1984.

39. Wilkinson, E.J., Schuettke, C.M., Ferrier, C.M., Franzini, D.A., Bland, K.I. : Fine needle aspiration of breast masses. An analysis of 276 aspirates. *Acta Cytologica*, 33 (5) : 613 - 619, 1989.
 40. Winship, T. : Aspiration biopsy of breast cancers by pathologist. *Am. J. Clin. Pathol.* 52 : 438-440, 1969.
 41. Wollenberg, N.J., Caya, J.G., Clowry, L.J. : Fine needle aspiration cytology of the breast. A review of 321 cases with statistical evaluation. *Acta Cytologica*, 29 (3) : 425 - 429, 1985.
 42. World Health Organization, International Histological Classification of Tumours, No.2, Histological typing of breast tumours, Second edition, Geneva, 1981.
 43. Zajdela, A., Ghossein, N.A., Pilleron, J.P. and Ennuyer, A. : The value of aspiration cytology in the diagnosis of breast cancer, experience at the fondation curie. *Cancer*, 35 : 499 - 506, 1975.
 44. Zajicek, J., Casperssan, T., Jakoberson, P., Kudynowski, J., Linksh, J. & U.S. Krasovcc, M. : Cytologic diagnosis of mammary tumours from aspiration biopsy smears - comparison of cytologic and histologic findings in 2111 lesions and diagnostic use of cytophometry. *Acta Cytologica*, 14 : 370-376, 1970.
-